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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,564	09/23/2003	Nicholas Michael Morton	674543-2004	3906

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EXAMINER	
MCMILLIAN, KARA RENITA	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
02/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,564	MORTON ET AL.	
	Examiner	Art Unit	
	KARA R. MCMILLIAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 18-53* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 27-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *14,18-26,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-21-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United Kingdom on March 23, 2001. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Response to Amendment

Applicant's amendments to the claims submitted on December 3, 2008 have been entered. Applicants have amended claims 14, 18, 20, 22, 23, 26, 52 and 53. Claims 1-13 and 27-51 are withdrawn. Claims 15-17 are canceled. Claims 14, 18-26, and 52-53 are presented for examination.

Response to Arguments

Due to Applicants amendment of claim 53, the rejection under 35 USC 112 first paragraph has been withdrawn. The rejection of claim 18 under 35 USC 112 second paragraph has also been withdrawn due to Applicants amendment of said claim.

In view of Applicants amendments to the claims the previous rejections under 35 USC 102 (b) and 103 submitted in the office action sent out on September 3, 2008 are hereby withdrawn. Applicant's arguments with respect to claims 14, 18-26 and 52-53 have been considered but are moot in view of the withdrawal of the rejections.

New rejections of claims 14, 18-26 and 52-53 necessitated by Applicants amendments are detailed below.

This action is made FINAL.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14,18-23, and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Nestler et al. U.S. Patent No. 4,920,115 (provided on IDS) as evidenced by Parasrampuria et al. U.S. 7,045,513 and Monder et al., 1993, Vitamins and Hormones, 47:187-271 (provided on IDS).

Claims 14, 18-23, and 52 of the instant application claim a method for reducing cardiovascular disease risk in an animal at risk comprising administering a pharmaceutically effective amount of an agent which directly inhibits 11β-HSD1 protein synthesis or 11β-HSD1 reductase activity such as steroids including 11-oxoprogesterone or 3β-hydroxyandrost-5-en-17-one.

Nestler et al. teach the administration of DHEA, also known as 3-beta-hydroxyandrost-5-en-17-one (see column 1 lines 52-53 of Parasrampuria et al.), for the treatment of atherosclerosis, angina, diabetes, obesity and congestive heart failure (see abstract). Nestler et al. further teach that administration of DHEA to human patients has

been found to lower serum LDL cholesterol levels, lower serum apoB levels, and not affect tissue sensitivity to insulin (see abstract). Nestler et al. discloses that the administration of DHEA decrease total cholesterol concentrations by 7.1% and mean serum LDL cholesterol concentration by 7.5% (see column 5 lines 50-53). Nestler et al. further discloses that the magnitude of serum cholesterol reduction by DHEA in the inventor's study represents an estimated 14% reduction in risk for the development of cardiovascular disease. Claims 1-4 of Nestler et al. claim a method of lowering low density lipoprotein (LDL) cholesterol concentrations in human beings, comprising the administration of a therapeutic dose of dehydroepiandrosterone (DHEA).

Table IV of Monder et al. identifies 3-beta-hydroxyandrost-5-en-17-one (DHEA) as a steroid capable of inhibiting 11β-HSD1 reductase activity (see page 196). Furthermore, claim 18 of the instant application specifically claims 3-beta-hydroxyandrost-5-en-17-one (DHEA) as an agent that reduces cardiovascular disease risk in an animal at risk by directly inhibiting 11β-HSD1 protein synthesis or 11β-HSD1 reductase activity. As such claims 14, 18, 20 and 52 are anticipated by Levine et al. as evidenced by Parasrampuria et al. and Monder et al.

Claims 19 and 21-23 are also anticipated by Levine et al. as evidenced by Parasrampuria et al. and Monder et al. since Levine et al. discloses an estimated 14% reduction in risk for the development of cardiovascular disease by the administration of 3-beta-hydroxyandrost-5-en-17-one (DHEA) and 3-beta-hydroxyandrost-5-en-17-one (DHEA) inhibits 11β-HSD1 reductase activity. The properties claimed in claims 19 and 21-23 of the instant application are inherent properties of 3-beta-hydroxyandrost-5-en-

17-one (DHEA) since progesterone reduces the risk of cardiovascular disease and inhibits 11β-HSD1 activity.

A previously discovered drug does not become patentable upon the discovery of a new property. The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Claims 14, 19-23 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Fruchart et al. (1999, Current Opinion in Lipidology, 10(3):245-257) as evidenced by Hermanowski-Vosatka et al. (2000, Biochemical and Biophysical Research Communications, Volume 279, pages 330-336).

Claims 14, 19-23 and 53 of the instant application claims a method for reducing cardiovascular disease risk in an animal comprising the administration of an agent that downregulates 11β-HSD1 protein synthesis from 11β-HSD1 mRNA.

Fruchart et al. teach that PPARα activators such as fibrates (e.g. fenofibrate) inhibit the development of atherosclerosis through their normolipidemic activities as well as through inhibition of vascular inflammation and thrombogenesis (see abstract and conclusion on page 254). Fruchart et al. teach that PPAR-α activation by fibrates (i.e. fenofibrate) leads to decreased hypertriglyceridemia by increasing lipoprotein lipase expression and deceasing apolipoprotein (apo) C-III expression; increased HDL

cholesterol; and reduced LDL cholesterol (see page 247 second paragraph). Fruchart et al. further teach that one of the major effects of PPAR-alpha activators on plasma lipid metabolism is to reduce triglyceride levels (see page 248). Fruchart et al further teach that in severe primary hypercholesterolemia, fenofibrate therapy decreased apo C-III (see page 249). Fibrate therapy increases HDL-cholesterol plasma levels by approximately 10-15% in hypertriglyceridemia, and hypercholesterolemia (see page 250).

Hermanowski-Vosatka et al. teach that PPARα agonists such as fenofibrate decrease 11β-HSD1 mRNA levels, 11β-HSD1 activity, and 11β-HSD1 protein levels (see results page 332-333). Thus the recited claims are anticipated since Fruchart et al. teach that PPARα agonists, which inhibit protein synthesis of 11β-HSD1 (as evidenced by Hermanowski-Vosatka et al.) reduce cardiovascular disease risk by inhibiting the development of atherosclerosis through their normolipidemic activities as well as through inhibition of vascular inflammation and thrombogenesis.

A previously discovered drug does not become patentable upon the discovery of a new property. The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nestler et al. U.S. Patent No. 4,920,115 (provided on IDS) as evidenced by Parasrampuria et al. U.S. 7,045,513 and Monder et al. (1993, Vitamins and Hormones, 47:187-271 provided on IDS) as applied to claims 14, 18-23, and 52 above and further in view of Kotelevtsev et al. (1997, PNAS, 94:14924-14929- provided on IDS).

Claims 24-25 of the instant application claim the method of instant claim 14 wherein the agent increases insulin sensitivity risk and improves glucose tolerance in an animal at risk of cardiovascular disease.

Nestler et al. as evidenced by Parasrampuria et al. and Monder et al. anticipate instant claim 14 as described above. Nestler et al. do not teach that DHEA increases insulin sensitivity risk or improves glucose tolerance in an animal at risk of cardiovascular disease.

Nestler et al. teach that unlike androgen therapy which results in decreased tissue sensitivity to insulin, DHEA administration had no effect on tissue sensitivity to insulin and insulin responsiveness was not assessed (see column 7 lines 24-30). Nestler et al. further discloses that it is however possible that DHEA administration

might alter insulin sensitivity if administered for a longer duration or to a group of individuals with pre-existing insulin resistance (see column 7 lines 32-36).

Kotelevtsev et al. teach that animals without 11β-HSD1 are resistant to the induction of hyperglycemia produced by diet as compared to animals that express 11β-HSD1 (see abstract and page 14927). Based on said disclosure of Kotelevtsev et al. it would be obvious to one of ordinary skill in the art that downregulation of 11β-HSD1 would improve glucose tolerance and increase insulin sensitivity since animals 11β-HSD1 null were resistant to hyperglycemia.

Since Monder et al. teach that DHEA decreases 11β-HSD1 activity and Kotelevtsev et al. teach that downregulation of 11β-HSD1 activity improves glucose tolerance and increase insulin sensitivity, DHEA would necessarily improve glucose tolerance and increase insulin sensitivity. As such claims 24-25 are rendered obvious.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nestler et al. U.S. Patent No. 4,920,115 (provided on IDS) as evidenced by Parasrampuria et al. U.S. 7,045,513 and Monder et al. (1993, Vitamins and Hormones, 47:187-271 provided on IDS) in view of Kotelevtsev et al. (1997, PNAS, 94:14924-14929 provided on IDS) as applied to claims 24-25 above and further in view of Fruchart et al. (1999, Current Opinion in Lipidology, 10(3):245-257).

Nestler et al. as evidenced by Parasrampuria et al. and Monder et al. in view of Kotelevtsev et al., as applied to claims 24-25 is as set forth above.

Nestler et al. (as evidenced by Parasrampuria et al. and Monder et al.) in view of Kotelevtsev et al. do not disclose the use of a PPARα agonist in conjunction with an agent that reduces 11β-HSD1 activity in a method for the promotion of an atheroprotective lipid profile.

Fruchart et al. teach that PPARα activators such as fibrates (e.g. fenofibrate) inhibit the development of atherosclerosis through their normolipidemic activities as well as through inhibition of vascular inflammation and thrombogenesis (see abstract and conclusion on page 254).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Nestler et al. which teach the administration of DHEA for the treatment of atherosclerosis and that administration of DHEA to human patients has been found to lower serum LDL cholesterol levels with the teachings of Fruchart et al. which teach that fibrates such as fenofibrate which are PPARα agonists inhibit the development of atherosclerosis through is ability to improve plasma lipid profile and decrease vascular wall inflammation (see abstract). An ordinary skilled artisan would be motivated to use both types of drugs in the treatment or reduction of atherosclerosis in order to produce an increased treatment outcome. The examiner respectfully points out the following from MPEP 2144.06:

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose .... [T]he idea of combining them flows logically from

their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980).

As such claim 26 is rendered obvious in view of the recited prior art references.

Conclusions

Claims 14, 18-26, and 52-53 are rejected. Claims 1-13 and 27-51 are withdrawn. Claims 15-17 are canceled. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARA R. MCMILLIAN whose telephone number is

(571)270-5236. The examiner can normally be reached on Monday-Thursday from 8:30 am- 6:00 pm and every other Friday from 8:30 am- 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kara R. McMillian/
Examiner, Art Unit 1617

KRM

/SREENI PADMANABHAN/
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